86215 Hominidae
Super Taxa:
Animals; Chordates; Vertebrates; Mammals; Primates; Humans

9/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11542384 BIOSIS Number: 98142384
Identification of potential CTL epitopes of tumor-associated antigen MAGE-1 for five common HLA-A alleles
Celis E; Fikes J; Wentworth P; Sidney J; Southwood S; Maewal A; Del Guercio M-F; Sette A; Livingston B
3525 John Hopkins Court, Cytel Corp., San Diego, CA 92121, USA
Molecular Immunology 31 (18). 1994. 1423-1430.
Full Journal Title: Molecular Immunology
ISSN: 0161-5890
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 007 Ref. 098941
Identification of CTL epitopes for tumor-specific responses is important for the development of immunotherapies to treat cancer patients. We have developed a strategy to identify potential CTL epitopes based on screening of sequences of target proteins for presence of specific motifs recognized by the most common HLA-A alleles, and identification of high affinity binding peptides using in vitro quantitative assays. A systematic analysis using the sequence of the product of the tumor-associated MAGE-1 gene has been carried out. All possible peptides of nine and ten residues, containing binding motifs for HLA-A1, -A2.1, A-3.2, -A11 and -A24 were synthesized and tested for binding using a quantitative assay. Out of 237 possible peptide/MHC combinations, 47 cases demonstrated good binding affinity (K-d ltoreq 500 nM). Several peptides were identified as good MHC binders for each one of the five HLA-A alleles studied (five for HLA-A1, 11 for HLA-A2.1, 10 for HLA-A3.2, 16 for HLA-A11 and five for HLA-A24. Furthermore, eight of these peptides were found to bind well to more than one HLA-A allele. These results have important implications for the development of immunotherapeutic vaccines to treat malignant melanoma.
Descriptors/Keywords: RESEARCH ARTICLE; HUMAN; CYTOTOXIC T-LYMPHOCYTE EPITOPES; PEPTIDE-HLA INTERACTION; IMMUNOTHERAPEUTIC VACCINE IMPLICATIONS; MALIGNANT MELANOMA
Concept Codes:
*02508 Cytology and Cytochemistry-Human
*03508 Genetics and Cytogenetics-Human
*10054 Biochemical Methods-Proteins, Peptides and Amino Acids
*10058 Biochemical Methods-Carbohydrates
*10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines
*10064 Biochemical Studies-Proteins, Peptides and Amino Acids
*10068 Biochemical Studies-Carbohydrates
*10506 Biophysics-Molecular Properties and Macromolecules
*15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System
*24003 Neoplasms and Neoplastic Agents-Immunology
*34502 Immunology and Immunochemistry-General; Methods
*34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
10052 Biochemical Methods-Nucleic Acids, Purines and Pyrimidines
10504 Biophysics-General Biophysical Techniques
12512 Pathology, General and Miscellaneous-Therapy (1971-)

18506 Integumentary System-Pathology
22005 Pharmacology-Clinical Pharmacology (1972-)
22018 Pharmacology-Immunological Processes and Allergy
22020 Pharmacology-Integumentary System, Dental and Oral Biology
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
Biosystematic Codes:
86215 Hominidae
Super Taxa:
Animals; Chordates; Vertebrates; Mammals; Primates; Humans

9/9/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11493063 BIOSIS Number: 98093063
A peptide encoded by human gene MAGE-3 and presented by HLA-A2 induces cytolytic T lymphocytes that recognize tumor cells expressing MAGE-3
Van Der Bruggen P; Bastin J; Gajewski T; Coulie P G; Boel P; De Smet C; Traversari C; Townsend A; Boon T
Ludwig Inst. Cancer Res., Brussels Branch, 74 Avenue Hippocrate -UCL 74.59, B-1200 Brussels, Belgium
European Journal of Immunology 24 (12). 1994. 3038-3043.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 005 Ref. 063473
The human MAGE-3 gene is expressed in many tumors of several histological types but it is silent in normal tissues, with the exception of testis. Antigens encoded by MAGE-3 may, therefore, be useful targets for specific anti-tumor immunization of cancer patients. We reported previously that MAGE-3 codes for an antigenic peptide recognized on a melanoma cell line by autologous cytolytic T lymphocytes (CTL) restricted by HLA-A1. Here we report that the MAGE-3 gene also codes for another antigenic peptide that is recognized by CTL restricted by HLA-A2. MAGE-3 peptides bearing consensus anchor residues for HLA-A2 were synthesized and tested for binding. T lymphocytes from normal individuals were stimulated with autologous irradiated lymphoblasts pulsed with each of three peptides that showed strong binding to HLA-A2. Peptide FLWGPRALV was able to induce CTL. We obtained CTL clones that recognized not only HLA-A2 cells pulsed with this peptide but also HLA-A2 tumor cell lines expressing the MAGE-3 gene. The proportion of melanoma tumors expressing this antigen should be approximately 32% in Caucasian populations, since 49% of individuals carry the HLA-A2 allele and 65% of melanomas express MAGE-3.
Descriptors/Keywords: RESEARCH ARTICLE; CHROMOSOME X; MAJOR HISTOCOMPATIBILITY COMPLEX; ANALYTICAL METHOD
Concept Codes:
*02508 Cytology and Cytochemistry-Human
*03508 Genetics and Cytogenetics-Human
*15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
*15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System
*24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
*34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10068 Biochemical Studies-Carbohydrates

86215 Hominidae
Super Taxa:
Animals; Chordates; Vertebrates; Mammals; Primates; Humans

9/9/5 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

9952579 EMBASE No: 96118485
Tumor escape from immune recognition: Loss of HLA-A2 melanoma cell surface expression is associated with a complex rearrangement of the short arm of chromosome 6
Maeurer M.J.; Gollin S.M.; Storkus W.J.; Swaney W.; Karbach J.; Martin D.; Castelli C.; Salter R.; Knuth A.; Lotze M.T.
Department of Medical Microbiology, Institutshochhaus Augustusplatz, D-55101 Mainz Germany
Clinical Cancer Research (USA) , 1996, 2/4 (641-652) CODEN: CCREF
ISSN: 1078-0432
LANGUAGES: English SUMMARY LANGUAGES: English
SUBFILES: 016; 022; 026
Specific CD8+ CTL recognition of melanoma requires expression of MHC class I molecules as well as melanoma-associated peptide epitopes. Human melanoma cells may escape immune recognition by a variety of means, including global or allelic down-regulation of MHC class I molecules. Stable MHC class I cell surface expression requires delivery of cytosolic peptides into the endoplasmic reticulum by the peptide transporter molecules TAP1 and TAP2, with peptides subsequently transported to the cell surface in complexes containing MHC class I heavy chain and beta2-microglobulin. We have evaluated a series of mechanisms resulting in MHC class I down-regulation in a human melanoma cell line, Mz18, typed as HLA-A2+, A3+, B7+, B57+ Cw1+, and Cw6+ by genomic PCR analysis. The melanoma cell line Mz18 exhibits a global down-regulation of MHC class I heavy chain transcripts; beta2-microglobulin; the proteasome subunits LMP2/7, involved in generating cytosolic peptide fragments; and the peptide transporter molecules TAP1 and TAP2, involved in peptide transport from the cytosol into the endoplasmic reticulum. IFN-gamma treatment of Mz18 melanoma cells leads to up-regulation of LMP2/7 and TAP1/2, as well as to up-regulation of HLA-B and HLA-C MHC loci alleles, but not HLA-A2 or HLA-A3. Karyotypic analysis and fluorescence in situ hybridization with chromosome 6 and MHC class I-specific probes showed complex rearrangement of one chromosome 6 involving the MHC class I locus on 6p and translocation of 6q to the long arm of chromosome 19. To evaluate the capability of melanoma Mz18 to present tumor-specific peptides to HLA-A2-restricted, melanoma-specific CTLs, we restored HLA-A2 surface expression by retroviral-mediated transfer of functional HLA-A2 cDNA. Melanoma peptides could only be presented and recognized by CTLs if the HLA-A2-transfected Mz18 cell line was first treated with IFN-gamma, thereby restoring LMP2/7 and TAP1/2 expression and function. Because several melanoma antigens recognized by T cells have been reported to be presented by HLA-A2 (MART-1/Melan-A, tyrosinase, gp100, and MAGE-3), the loss of HLA-A2 molecules may represent an important mechanism by which many melanomas evade immune recognition. These findings suggest that patients entering clinical trials for immunotherapy with melanoma vaccines should be carefully examined for tumor cell allelic MHC class I loss and whether such MHC class I antigen down-regulation can be restored by cytokines.

EMTAGS:

Cancer 0306; Genetic engineering 0108; Heredity 0137; Mammal 0738; Human 0888; Controlled study 0197; Human tissue, cells or cell components 0111; Priority journal 0007; Article 0060
DRUG DESCRIPTORS:
*membrane antigen--endogenous compound--ec; *HLA A2 antigen--endogenous compound--ec; *melanoma antigen--endogenous compound--ec; *gamma interferon
MEDICAL DESCRIPTORS:
*melanoma cell; *chromosome rearrangement; *chromosome 6p tumor cell line; immunogenicity; down regulation; fluorescence in situ hybridization; human; controlled study; human cell; priority journal; article
EMCLAS DRUG CODES:
03700000000

CAS REGISTRY NO.: 82115-62-6 (gamma interferon)

9/9/6 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

9862005 EMBASE No: 96027358
Detection of naturally processed and HLA-A1-presented melanoma T-cell epitopes defined by CD8+ T-cells' release of granulocyte-macrophage colony-stimulating factor but not by cytolysis
Maeurer M.J.; Martin D.; Elder E.; Storkus W.J.; Lotze M.T.
Department of Medical Microbiology, University of Mainz, Hochhaus Augustusplatz, D-55101 Mainz Germany
Clinical Cancer Research (USA) , 1996, 2/1 (87-95) CODEN: CCREF ISSN: 1078-0432
LANGUAGES: English SUMMARY LANGUAGES: English
SUBFILES: 013; 016; 026
Several antigens, including the products encoded by the genes MAGE-1 and MAGE-3, are recognized on human melanoma cells by HLA-A1, HLA-A2, or HLA-Cw(*)1601(*)-restricted T cells on autologous or HLA-matched melanoma cell lines, T-cell recognition of naturally processed MHC class I-presented peptides, or alternatively synthetic peptides derived from MAGE-1 or MAGE-3, leads to cytokine release as well as to a cytotoxic T-cell response in these antimelanoma-directed polyclonal or clonal effector T-cell populations, Recent reports suggest that the activity of T lymphocytes infiltrating melanoma in vivo appears to be impaired, We report here tile characterization of the in vitro (in the presence of 6000 IU interleukin 2) expanded tumor-infiltrating lymphocyte (TIL) T-cell line PM2-B2 derived from a patient with rapidly progressing and therapy-resistant head and neck melanoma, The TIL cell line PM2-B2 did not lyse, but instead released granulocyte-macrophage colony-stimulating factor in response to the autologous tumor or HLA-A1-matched allogeneic tumor cell lines, The TIL line PM2-B2 did not kill the MHC class I natural killer! lymphokine-activated killer target cell lines Daudi or K562, The fine specificity of the TIL line PM2-B2 restricted by HLA-A1 was further characterized by evaluating specific granulocytc-macrophage colony-stimulating factor release in response to MHC class I-eluted peptides derived from HLA-A1+ melanoma cell lines, TIL PM2-B2 failed to recognize the recently described HLA-A1-presented peptides derived from the gene products encoded by MAGE-1 or MAGE-3, PCR-based analysis of the freshly harvested tumor from patient PM2-B2 revealed the presence of message for the melanoma-associated gene products MAGE-1 and MAGE-3, but not for tyrosinase or MART-1/MELAN-A. Acid elution and high performance

liquid chromatography fractionation of MHC class I-presented peptides from HLA-A1-matched melanoma cell lines 397 or 888 revealed that TIL PM2-B2 recognized at least three distinct peptide epitopes eluting in high performance liquid chromatographic bioactive fractions 5/6, 36, and 51/52, These bioactive peaks appeared to be shared among HLA-A1+ melanoma cell lines. We suggest, based on this report, that HLA-A1-presented melanoma-derived peptides (other than those previously reported peptides derived from MAGE-1 or MAGE-3) may represent targets for TIL recognition as defined by cytokine release, but not cytotoxicity. Such an immune response differentially defined by cytokine release, but absent cytotoxic functions, may either reflect the impaired cytolytic function of the TIL population or reflect the inherent nature of HLA-A1-presented melanoma T-cell epitopes leading to cytokine release, but not to a cytotoxic T-cell response. Additionally, this report suggests that the individual T-cell immune response to melanoma may be rather complex, involving diverse T-cell effector functions (e.g., cytotoxicity or cytokine release), each of which should be evaluated in studies of antitumor-specific T-cell reactivity.
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BRAND NAME/MANUFACTURER NAME: USA cetus

EMTAGS:
Cancer 0306; Blood and hemopoietic system 0927; Lymphatic system 0929; Mammal 0738; Human 0888; Controlled study 0197; Case report 0151; Human tissue, cells or cell components 0111; Priority journal 0007; Article 0060
DRUG DESCRIPTORS:
*cd8 antigen--endogenous compound--ec; *HLA A1 antigen--endogenous compound --ec; *granulocyte macrophage colony stimulating factor--endogenous compound--ec; *interleukin 2
MEDICAL DESCRIPTORS:
*melanoma; *t lymphocyte; *tumor associated leukocyte; *antigen recognition epitope; human; controlled study; case report; human cell; priority journal ; article
EMCLAS DRUG CODES:
03700000000

CAS REGISTRY NO.: 85898-30-2 (interleukin 2)

9/9/7 (Item 1 from file: 149)
DIALOG(R)File 149:IAC(SM) Health & Wellness DB(SM)

01480019 SUPPLIER NUMBER: 15250567 (THIS IS THE FULL TEXT)
Newly cloned gene could aid in treating melanoma. (MART-1, U.S. National Cancer Institute)
Cancer Researcher Weekly, p11(1)
May 9, 1994
PUBLICATION FORMAT: Newsletter ISSN: 1071-7226 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Academic; Professional
WORD COUNT: 512 LINE COUNT: 00050

TEXT:

Gene Discovery

U.S. National Cancer Institute (NCI) scientists have identified, cloned and sequenced a gene coding for one of the principal proteins that elicit natural immunity against melanoma, a cancer of the pigment-forming cells of the skin. Potentially this gene, MART-1, or its corresponding protein antigen, could be used to produce a melanoma vaccine.

Steven A. Rosenberg, M.D., Ph.D., Yutaka Kawakami, M.D., and their colleagues at NCI reported their findings in the April 26, 1994, issue of the Proceedings of the National Academy of Sciences.

The MART-1 protein is an effective antigen only in individuals expressing an immune marker known as HLA-A2. But since this marker is very common, treatment based on MART-1 could have wide use.

Identifying tumor-associated antigens has been a major goal of cancer research. The hope is that such antigens could be used to develop vaccines or other specific cancer therapies. Melanoma has been a particular target of such research, both because the advanced disease is deadly and difficult to treat, and because it seems to be unusually responsive to immunologic changes.

Rosenberg and his co-workers discovered in 1988 that certain immune cells found in tumors have potent activity against the tumors from which they derive. These tumor -infiltrating lymphocytes, or TIL, are able to destroy the tumor cells. They have been shown to shrink tumors in more than one-third of melanoma patients.

"The ability of TIL to mediate regression of advanced melanoma suggests that the antigens the TIL recognize play an important role in the immune response against these cancers," Rosenberg said. "For that reason, we wanted to identify the antigens. Doing so could give us important information about the body's natural anti-tumor defenses and provide a valuable tool to use in developing cancer treatments."

Using a complex multi-step procedure, the investigators identified and cloned (copied) a DNA sequence coding for a protein recognized by melanoma -derived TIL. The researchers gave this sequence, which was unlike any registered in an established database, the name MART-1, for Melanoma Antigen Recognized by T Cells -1.

Testing showed the gene for MART-1 to be active in human melanocytes (normal pigment-forming cells) and in most melanoma cell lines. Retinal tissue, which contains melanocytes, also tested positive, but other normal tissues did not. The investigators concluded that MART-1 is a previously undescribed antigen expressed on cells from skin and retina and also on many melanoma cells.

Since pigment cells in skin and retina are not essential for any life function, immunotherapy directed against MART-1 could potentially provide benefit without causing major toxicity. Rosenberg's group has now identified a 9-amino-acid peptide within MART-1 that appears to be a common antigen for many melanoma-specific TIL and that might aid in developing such immunotherapy.

MART-1 appears to be a non-mutated "self" peptide. Since the immune system is normally tolerant, or non -reactive, to "self" antigens (i.e., antigens that identify a specific individual), researchers working with MART-1 will need to learn more about the particular conditions that permit such tolerance to be broken.

The antigens that correspond to the DNA sequences identified by Rosenberg's team are unique in that they are recognized by naturally occurring TIL derived from melanomas. The NCI scientists have shown that their TIL do not recognize other known melanoma-associated antigens, such as MAGE-1.

"The identification of genes encoding cancer -associated antigens provides a solid scientific base for the future development of immunotherapies," Rosenberg said.

DESCRIPTORS: Melanoma--Genetic aspects; Tumor-infiltrating lymphocytes--Physiological aspects; Immunotherapy--Research
FILE SEGMENT: HI File 149

9/9/11 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

174717 DBA Accession No.: 95-01538
Tumor antigens recognized by cytotoxic T-lymphocytes: hope for specific immunotherapy - tumor antigen characterization using tyrosinase gene, for potential cancer immunotherapy by genetic immunization (conference abstract)
AUTHOR: Brichard V; van der Bruggen P; Van Pel A; De Palen E; Coulie P; Boon T
CORPORATE AFFILIATE: Ludwig-Inst.Cancer-Res.
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels Branch, Brussels B-1200, Belgium.
JOURNAL: Gene Ther. (1, Suppl.2, S3) 1994
CODEN: 4352W
CONFERENCE PROCEEDINGS: Second Meeting of European Working Group on Human Gene Transfer and Therapy, London, UK, 18-21 November, 1994.
LANGUAGE: English
ABSTRACT: Genes encoding antigens recognized on tumors by autologous cytotoxic T-lymphocytes (CTL) led to the characterization of a family of 12 genes, named MAGE. By stimulating T-lymphocytes from normal individuals with a MAGE-3 peptide that showed strong binding to HLA-A2, CTL clones were obtained that recognized not only HLA-A2 cells pulsed with the peptide, but also HLA-A2 tumor cell-lines expressing gene MAGE-3. Tumor antigens expressed by a majority of melanomas and presented by HLA-A2 are derived from the tyrosinase (TY, EC-1.14.18.1) gene and from a new gene, named Melan-A. Unlike the MAGE genes, expression of the latter genes is restricted to melanomas and, among normal tissues, to melanocytes. The TY gene encodes an additional epitope presented by HLA-B44. The relevant non-apeptide is recognized by the CTL only in the context of the HLA-B44-03 subtype. Patients liable to benefit from specific immunization can be identified upon the analysis of the tumor antigens expressed by the tumor together with HLA typing, and antigens can be modified for optimal genetic immunization for cancer immunotherapy. (2 ref)
E.C. NUMBERS: 1.14.18.1
DESCRIPTORS: melanoma tumor-associated antigen characterization, tyrosinase gene, cytotoxic T-lymphocyte, pot. cancer immunotherapy, genetic immunization gene therapy enzyme EC-1.14.18.1 recombinant vaccine (Vol.14, No.3)
SECTION: PHARMACEUTICALS-Clinical Genetic Techniques; PHARMACEUTICALS-Vaccines; GENETIC ENGINEERING AND FERMENTATION-Nucleic Acid Technology (D7,D4,A1)

9/9/12 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

14378844 Genuine Article#: TJ222 Number of References: 22
Title: HUMAN NEOPLASMS ELICIT MULTIPLE SPECIFIC IMMUNE-RESPONSES IN THE AUTOLOGOUS HOST
Author(s): SAHIN U; TURECI O; SCHMITT H; COCHLOVIUS B; JOHANNES T; SCHMITS R; STENNER F; LUO GR; SCHOBERT I; PFREUNDSCHUH M
Corporate Source: UNIV SAARLAND,SCH MED,MED KLIN & POLIKLIN/D-66421 HOMBURG//GERMANY/; UNIV SAARLAND,SCH MED,MED KLIN & POLIKLIN/D-66421

HOMBURG//GERMANY/
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 1995, V92, N25 (DEC 5), P11810-11813
ISSN: 0027-8424
Language: ENGLISH Document Type: ARTICLE
Geographic Location: GERMANY
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: MULTIDISCIPLINARY SCIENCES
Abstract: Expression of cDNA libraries from human melanoma, renal cancer, astrocytoma, and Hodgkin disease in Escherichia coli and screening for clones reactive with high-titer IgG antibodies in autologous patient serum lead to the discovery of at least four antigens with a restricted expression pattern in each tumor, Besides antigens known to elicit T-cell responses, such as MAGE-1 and tyrosinase, numerous additional antigens that were overexpressed or specifically expressed in tumors of the same type were identified, Sequence analyses suggest that many of these molecules, besides being the target of a specific immune response, might be of relevance for tumor growth, Antibodies to a given antigen were usually confined to patients with the same tumor type. The unexpected frequency of human tumor antigens, which can be readily defined at the molecular level by the serological analysis of autologous tumor cDNA expression cloning, indicates that human neoplasms elicit multiple specific immune responses in the autologous host and provides diagnostic and therapeutic approaches to human cancer.
Descriptors--Author Keywords: HUMAN TUMOR ANTIGENS ; ANTIBODIES
Identifiers--KeyWords Plus: GENE; LYMPHOCYTES; EXPRESSION; PEPTIDE
Research Fronts: 93-1469 002 (MHC CLASS-I MOLECULES; PEPTIDE PRESENTATION; CYTOTOXIC T-LYMPHOCYTES; ANTIGEN PROCESSING)
93-1267 001 (CANCER VACCINES; RANDOMIZED PHASE-II TRIAL OF HIGH-DOSE INTERLEUKIN-2; ADOPTIVE CELLULAR THERAPY; HLA-A2 MATCHED ALLOGENEIC MELANOMA-CELLS)
93-1652 001 (HUMAN CARBONIC ANHYDRASE-II; COMPLEX INHIBITORS CONTAINING METAL-IONS; BOVINE ABOMASUM)
Cited References:
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MANDELBOIM O, 1994, V369, P67, NATURE
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Self Reference:

SAHIN U, 1995, V92, P11810, P NAS US

9/9/13 (Item 2 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

14356130 Genuine Article#: TF625 Number of References: 24
Title: HUMAN ESOPHAGEAL CARCINOMAS FREQUENTLY EXPRESS THE TUMOR-REJECTION ANTIGENS OF MAGE GENES
Author(s): INOUE H; MORI M; LI J; MIMORI K; HONDA M; NAKASHIMA H; MAFUNE K; TANAKA Y; AKIYOSHI T
Corporate Source: KYUSHU UNIV,MED INST BIOREGULAT,DEPT SURG,4546 TSURUMIBARU/BEPPU/OITA 874/JAPAN/; KYUSHU UNIV,MED INST BIOREGULAT,DEPT SURG/BEPPU/OITA 874/JAPAN/; SAITAMA CANC CTR,DEPT SURG/INA/SAITAMA/JAPAN/
Journal: INTERNATIONAL JOURNAL OF CANCER, 1995, V63, N4 (NOV 15), P523-526
ISSN: 0020-7136
Language: ENGLISH Document Type: ARTICLE
Geographic Location: JAPAN
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: ONCOLOGY
Abstract: The human genes MAGE-1 and -3 encode melanoma peptide antigens that are recognized by autologous cytotoxic T lymphocytes. Tumors expressing MAGE genes are potential targets for cancer immunotherapy, because MAGE genes are expressed only in tumor tissue and not in any normal tissue except testis and placenta. However, little is known about MAGE gene expression in human esophageal carcinoma. The purpose of this study was therefore to analyze MAGE gene status in human esophageal carcinoma. We studied the expression status of these genes in 42 surgical samples and in 12 cell lines of human esophageal carcinoma using the reverse transcription polymerase chain reaction (RT-PCR). Various clinicopathological factors were also analyzed. No MAGE gene expression was seen in any of the 42 normal esophageal tissue specimens. In contrast, tumor tissue expressed MAGE-1, -2, and -3 in 26, 18 and 24 specimens, respectively. Thirty-three of 42 tumors expressed at least one MAGE gene. Significant clinicopathologic differences between the tumors were not observed, regardless of the presence or absence of MAGE gene expression. In cell lines, MAGE-1, -2, and -3 gene expression was recognized in 5, 4 and 4 cell lines, respectively. This study demonstrates that MAGE genes are frequently expressed in clinical samples as well as in cell lines of esophageal carcinoma. The identification of MAGE genes, therefore, may open up a new modality of treatment, namely specific immunotherapy, for patients with esophageal carcinoma. (C) 1995 Wiley-Liss, Inc.
Identifiers--KeyWords Plus: CYTOLYTIC T-LYMPHOCYTES; HUMAN-MELANOMA; CODES
Research Fronts: 93-1267 001 (CANCER VACCINES; RANDOMIZED PHASE-II TRIAL OF HIGH-DOSE INTERLEUKIN-2; ADOPTIVE CELLULAR THERAPY; HLA-A2 MATCHED ALLOGENEIC MELANOMA-CELLS)
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WEYNANTS P, 1994, V56, P826, INT J CANCER
Self Reference:
INOUE H, 1995, V63, P523, INT J CANC

9/9/14 (Item 3 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

14287704 Genuine Article#: TB816 Number of References: 21
Title: THE EXPRESSION OF TUMOR-REJECTION ANTIGEN MAGE GENES IN HUMAN GASTRIC-CARCINOMA
Author(s): INOUE H; MORI M; HONDA M; LI J; SHIBUTA K; MIMORI K; UEO K; AKIYOSHI T
Corporate Source: KYUSHU UNIV,MED INST BIOREGULAT,DEPT SURG,KYUSHU UNIV 69/BEPPU 874//JAPAN/; KYUSHU UNIV,MED INST BIOREGULAT,DEPT SURG/BEPPU874//JAPAN/; OITA PREFECTURAL HOSP,DEPT SURG/OITA//JAPAN/
Journal: GASTROENTEROLOGY, 1995, V109, N5 (NOV), P1522-1525
ISSN: 0016-5085
Language: ENGLISH Document Type: ARTICLE
Geographic Location: JAPAN
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: GASTROENTEROLOGY AND HEPATOLOGY
Abstract: Background & Aims: The genes MAGE-1 and MAGE-3 both encode melanoma peptide antigens recognized by major histocompatibility complex-restricted cytotoxic T lymphocytes. The antigens may be a target for immunotherapy. There is, however, little information on the expression of these genes in gastric carcinomas. Therefore, the expression of MAGE genes in gastric carcinomas was evaluated. Methods: The expression of MAGE-1, MAGE-2, and MAGE-3 genes in tumors and corresponding normal tissue specimens was studied using a reverse-transcription polymerase chain reaction. The results were analyzed according to clinicopathologic factors of the tumor. Results: In the 68 gastric carcinomas studied, MAGE-1, MAGE-2, and MAGE-3 messenger RNA were detected in 41%, 31%, and 38%, respectively. Fifty percent of the gastric carcinomas expressed at least one of the MAGE genes, Messenger RNA for the three MAGE proteins was not detected in normal gastric tissue, MAGE gene expression in gastric carcinomas was not associated with a significant clincopathology of the tumor. However, gene expression was lower in mucinous carcinomas (3 of 10), Conclusions: MAGE-1, MAGE-2, and MAGE-3 are expressed in a high percentage of gastric carcinomas, These tumor rejection antigens may

provide tumor-specific targets for immunotherapy,
Identifiers--KeyWords Plus: CYTOLYTIC LYMPHOCYTES-T; HUMAN-MELANOMA; CODES
Research Fronts: 93-1267 001 (CANCER VACCINES; RANDOMIZED PHASE-II TRIAL OF HIGH-DOSE INTERLEUKIN-2; ADOPTIVE CELLULAR THERAPY; HLA-A2 MATCHED ALLOGENEIC MELANOMA-CELLS)
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WEYNANTS P, 1994, V56, P826, INT J CANCER

Self Reference:

INOUE H, 1995, V109, P1522, GASTROENTY

9/9/15 (Item 4 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

14278158 Genuine Article#: TA532 Number of References: 15
Title: ESTABLISHMENT OF AN ENZYME-LINKED-IMMUNOSORBENT-ASSAY (ELISA) FOR MEASURING CELLULAR MAGE-4 PROTEIN ON HUMAN CANCERS

Author(s): SHICHIJO S; TSUNOSUE R; KUBO K; KURAMOTO T; TANAKA Y; HAYASHI A; ITOH K
Corporate Source: KURUME UNIV,SCH MED,DEPT IMMUNOL/KURUME/FUKUOKA830/JAPAN/ ; KURUME UNIV,SCH MED,DEPT IMMUNOL/KURUME/FUKUOKA830/JAPAN/; KURUME UNIV,SCH MED,DEPT INTERNAL MED 1/KURUME/FUKUOKA 830/JAPAN/; KURUME UNIV,SCH MED,DEPT SURG 1/KURUME/FUKUOKA 830/JAPAN/

Journal: JOURNAL OF IMMUNOLOGICAL METHODS, 1995, V186, N1 (OCT 12), P 137-149
ISSN: 0022-1759
Language: ENGLISH Document Type: ARTICLE
Geographic Location: JAPAN
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: IMMUNOLOGY

Abstract: The MAGE genes encoding tumor-rejection antigens are expressed on various human cancers. An enzyme-linked immunosorbent assay (ELISA) was established for measuring cellular MAGE-4 protein (MAGE-4a and/or -4b) expressed on human tumor cells using a monoclonal antibody (mAb) and polyclonal Ab to recombinant MAGE-4b protein. Both the R5 mAb (IgG1) and the polyclonal Ab recognized a 45 kDa protein in extracts of MAGE-4 mRNA positive cancers, and showed no apparent cross-reactivity to the

other MAGE gene products (MAGE-1, -2, -3, -6, and -12) by the immunoblot analyses. The R5 mAb and the polyclonal Ab primarily recognized one (the position 119-133) and two oligopeptides (the positions 119-133 and 259-273), respectively, among a series of 31 different MAGE-4b oligopeptides. The amino acid sequences of these two peptides were identical to those of MAGE-4a and -4b, but differed from those of all the other MAGE proteins (MAGE-1, -2, -3, -6, and -12). Substitution of glycine for amino acid in position 123 (arginine, R), 124 (lysine, K), 126 (R) or 128 (K) in a MAGE-4b oligopeptide of the position 119-132 severely decreased the reactivity of the R5 mAb to the oligopeptide. This ELISA also showed no apparent cross-reactivity with the other MAGE gene products (MAGE-1, -2 -3, -6, and -12). The minimum detectable level of MAGE-4 protein was determined to be 10 pg/well (100 pg/ml). The results suggest that this ELISA is a reliable and quantitative method to measure cellular MAGE-4 protein that is a potential target molecule for specific immunotherapy of human cancers.

Descriptors--Author Keywords: ANTI-MAGE-4 ANTIBODY ; ELISA ; MAGE-4 PROTEIN ; HUMAN TUMOR ; SPECIFIC IMMUNOTHERAPY

Identifiers--KeyWords Plus: CYTOLYTIC LYMPHOCYTES-T; HUMAN GENE MAGE-1; ANTIGEN

Research Fronts: 93-1267 001 (CANCER VACCINES; RANDOMIZED PHASE-II TRIAL OF HIGH-DOSE INTERLEUKIN-2; ADOPTIVE CELLULAR THERAPY; HLA-A2 MATCHED ALLOGENEIC MELANOMA-CELLS)

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Self Reference:

SHICHIJO S, 1995, V186, P137, J IMMUNOL M

9/9/16 (Item 5 from file: 434)

DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

14179813 Genuine Article#: RU971 Number of References: 30

Title: A FAMILY OF RAPIDLY EVOLVING GENES FROM THE SEX REVERSAL CRITICAL REGION IN XP21

Author(s): DABOVIC B; ZANARIA E; BARDONI B; LISA A; BORDIGNON C; RUSSO V; MATESSI C; TRAVERSARI C; CAMERINO G

Corporate Source: UNIV PAVIA,VIA FORLANINI 14/I-27100 PAVIA//ITALY/; UNIV PAVIA/I-27100 PAVIA//ITALY/; CNR,IST GENET BIOCHIM & EVOLUZIONIST/I-27100 PAVIA//ITALY/; IST SCI HS RAFFAELE,DIBIT,GENE THERAPY PROGRAM/I-45100 MILAN//ITALY/; UNIV SASSARI,IST ISTOL & EMBRIOL/SASSARI//ITALY/

Journal: MAMMALIAN GENOME, 1995, V6, N9 (SEP), P571-580

ISSN: 0938-8990
Language: ENGLISH Document Type: ARTICLE
Geographic Location: ITALY
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; GENETICS & HEREDITY; BIOTECHNOLOGY & APPLIED MICROBIOLOGY
Abstract: Patients with an intact SRY gene and duplications of portions of Xp21 develop as phenotypic females. We have recently mapped this sex reversal locus, DSS, to a 160-kb region of Xp21 that includes the adrenal hypoplasia congenita locus. To clone the gene(s) underlying DSS and AHC, we isolated expressed sequences from the region. Here we describe the characterization of two related genes. DAM10 and DAM6, expressed in adult testis and lung tumors. The predicted DAM10 and DAM6 proteins are 66% identical and are both highly similar to the MAGE family of tumor-associated antigens and to mouse necdin. Genes belonging to the MAGE superfamily, DAMs, MAGEs, and necdin, are likely to have originated from a common ancestor and to be subject to an unusually rapid evolution. The tumor-restricted expression of DAM proteins and their structural similarity to MAGE genes suggest that DAM peptides may be targets for active immunotherapy in lung cancer patients.
Identifiers--KeyWords Plus: ADRENAL HYPOPLASIA-CONGENITA; NUCLEOTIDE SUBSTITUTION; OVERDOMINANT SELECTION; GLYCEROL KINASE; EVOLUTION; CHROMOSOME; LOCI
Research Fronts: 93-6631 002 (MAJOR HISTOCOMPATIBILITY COMPLEX GENES; MHC CLASS-I; POSITIVE SELECTION)
93-1267 001 (CANCER VACCINES; RANDOMIZED PHASE-II TRIAL OF HIGH-DOSE INTERLEUKIN-2; ADOPTIVE CELLULAR THERAPY; HLA-A2 MATCHED ALLOGENEIC MELANOMA-CELLS)
93-4826 001 (PHYLOGENETIC POSITION; 18S RIBOSOMAL-RNA GENE SEQUENCE; ANAEROBIC THERMOPHILIC BACTERIA)
93-4847 001 (HETEROLOGOUS EXPRESSION; CHROMOSOMAL DNA; GENE ENCODING METHYLMALONYL-COENZYME-A MUTASE)
93-5593 001 (NEURONAL TARGETING DEFECT IN THE OLFACTORY SYSTEM; X-LINKED KALLMANN SYNDROME; MALE HYPOGONADOTROPIC HYPOGONADISM)
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9/9/17 (Item 6 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

13905548 Genuine Article#: RA145 Number of References: 14
Title: IDENTIFICATION AND INTRACELLULAR LOCATION OF MAGE-3 GENE-PRODUCT
Author(s): KOCHER T; SCHULTZTHATER E; GUDAT F; SCHAEFER C; CASORATI G; JURETIC A; WILLIMANN T; HARDER F; HEBERER M; SPAGNOLI GC
Corporate Source: SURG RES LAB,20 HEBELSTR/CH-4031 BASEL//SWITZERLAND/; SURG RES LAB/CH-4031 BASEL//SWITZERLAND/; UNIV BASEL,DEPT RES/BASEL//SWITZERLAND/; UNIV BASEL,DEPT SURG/BASEL//SWITZERLAND/; UNIV BASEL,DEPT PATHOL/BASEL//SWITZERLAND/; DIPARTIMENTO BIOTECNOL HS RAFFAELE/MILAN//ITALY/
Journal: CANCER RESEARCH, 1995, V55, N11 (JUN 1), P2236-2239
ISSN: 0008-5472
Language: ENGLISH Document Type: NOTE
Geographic Location: SWITZERLAND; ITALY
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: ONCOLOGY
Abstract: The human MAGE-3 gene encodes a melanoma antigenic epitope recognized by specific cytotoxic T lymphocytes, but its gene product has not been identified thus far, We produced a recombinant MAGE-3 gene product by expression cloning of the entire reading frame in the context of a fusion protein characterized by a 10-histidine tall, allowing purification by metal chelation on a nickel Sepharose column, The semipurified product was used to generate MAGE-3-specific monoclonal antibodies. One reagent could identify by immunoblotting the native MAGE-3 gene product as a M(r) 48,000 protein in lysates of cell lines showing evidence of MAGE-3 gene expression. No apparent cross-reactivity with recombinant or native MAGE-1 gene product was observed, Immunohistochemistry shows that, closely resembling the MAGE-1 gene product, MAGE-3 is a cytoplasmic protein.
Identifiers--KeyWords Plus: HUMAN-MELANOMA; ANTIGEN
Research Fronts: 93-1267 001 (CANCER VACCINES; RANDOMIZED PHASE-II TRIAL OF HIGH-DOSE INTERLEUKIN-2; ADOPTIVE CELLULAR THERAPY; HLA-A2 MATCHED ALLOGENEIC MELANOMA-CELLS)
93-1469 001 (MHC CLASS-I MOLECULES; PEPTIDE PRESENTATION; CYTOTOXIC T-LYMPHOCYTES; ANTIGEN PROCESSING)
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9/9/18 (Item 7 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

13790381 Genuine Article#: QR070 Number of References: 40
Title: CTL SPECIFIC FOR THE TYROSINASE AUTOANTIGEN CAN BE INDUCED FROM HEALTHY DONOR BLOOD TO LYSE MELANOMA-CELLS
Author(s): VISSEREN MJW; VANELSAS A; VANDERVOORT EIH; RESSING ME; KAST WM; SCHRIER PI; MELIEF CJM
Corporate Source: LEIDEN UNIV HOSP,DEPT IMMUNOHAEMATOL,POSTBUS 9600/2300 RC LEIDEN//NETHERLANDS/; LEIDEN UNIV HOSP,DEPT IMMUNOHAEMATOL/2300 RC LEIDEN//NETHERLANDS/; LEIDEN UNIV HOSP,BLOOD BANK/2300 RC LEIDEN//NETHERLANDS/; LEIDEN UNIV HOSP,DEPT CLIN ONCOL/2300 RC LEIDEN//NETHERLANDS/
Journal: JOURNAL OF IMMUNOLOGY, 1995, V154, N8 (APR 15), P3991-3998
ISSN: 0022-1767
Language: ENGLISH Document Type: ARTICLE
Geographic Location: NETHERLANDS
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: IMMUNOLOGY
Abstract: CTL that lyse melanoma cells were previously isolated from several melanoma patients. Such CTL recognize autologous proteins, indicating the occurrence of autoreactive T cells in melanoma patients. We have now raised CTL, using responding T lymphocytes from healthy donor blood, that lysed not only cells incubated with an HLA-A*0201-binding tyrosinase peptide but also melanoma cells endogenously processing and presenting the epitope. Our results suggest that autoreactive CTL precursors are present in healthy donor blood and can be activated in vitro with synthetic peptides presented on appropriate APCs. Therefore, tissue-specific, autoantigen-derived peptides might be useful in immunotherapy of both poorly and nonimmunogenic tumors.
Identifiers--KeyWords Plus: CYTOTOXIC LYMPHOCYTES-T; TUMOR-CELLS; GENE MAGE-1; ANTIGEN; PEPTIDE; VIRUS; RESPONSES; INDUCTION; RECEPTOR; LYMPHOMA
Research Fronts: 93-1267 002 (CANCER VACCINES; RANDOMIZED PHASE-II TRIAL OF HIGH-DOSE INTERLEUKIN-2; ADOPTIVE CELLULAR THERAPY; HLA-A2 MATCHED ALLOGENEIC MELANOMA-CELLS)
93-1222 001 (EXPRESSION CLONING; COS CELLS; IGE RECEPTOR)
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9/9/19 (Item 1 from file: 636)
DIALOG(R)File 636:IAC Newsletter DB(TM)

03195614
Cancer Vaccine: "A Polyvalent Melanoma Vaccine Induces a CD8 T Cell Response to MART-1 and MAGE-3 Peptides."
Vaccine Weekly May 27, 1996
ISSN: 1074-2921 WORD COUNT: 253
PUBLISHER: Charles W Henderson

S.R. Reynolds, S. Vukmanovic, R. Oratz, R.L. Shapiro and J.C. Bystryn. New York University Medical Center, New York, New York.

According to an abstract submitted by the authors to the 87th Annual Meeting of the American Association for Cancer Research, held April 20-24, 1996, in Washington, D.C., "Melanoma patients immunized with a polyvalent vaccine were assessed for their peripheral blood lymphocyte (PBL) responses to the melanoma peptides MART-1, MAGE-3 and a control peptide from falciparum malaria. The vaccine was prepared from shed melanoma antigens,

bound to alum, and administered s.c. every 3 weeks x 4 to 10 HLA-A2+ patients. The peptides studied are all HLA-A2 restricted. Seven (70%) of the patients had a significant T cell response to MART-1 and/or MAGE-3-pulsed A2+ melanoma targets compared to control peptide as measured by IFN-gamma release. Three patients responded to MART-1 and five to MAGE-3. The responses appeared to be vaccine induced since two patients studied in detail had no detectable peptide-specific cells before immunization. After treatment, both had a statistically significant increase in CD8 IFN-

gamma}}-secreting cells (400/10(6) PBL to MART-1 in one patient and 580/10(6) PBL to MAGE-3 in the other patient). The responses were abrogated by antibodies to CD8 or HLA-class I but not by anti-CD4, indicating they were CD8 mediated. These results show that a polyvalent vaccine can induce a CD8 response to MART-1 and MAGE-3, and provide direct evidence that these proteins can induce a T cell response in humans."

Subscription: $995 per year as of 6/94. Published 52 times per year. Contact Charles W Henderson, P.O. Box 830409, Birmingham, AL 35283-0409. Phone (800) 633-4931. FAX (205) 995-1567.

INDUSTRY: Medical and Health (MH)

9/9/20 (Item 2 from file: 636)
DIALOG(R)File 636:IAC Newsletter DB(TM)

03188069
Melanoma "Tumor Escape from Immune Recognition: Loss of HLA-A2 Melanoma Cell Surface Expression Is Associated with a Complex Rearrangement of the Short Arm of Chromosome 6(1)." Clinical Cancer Research, April 1996;2(4):641-652.
Vaccine Weekly May 20, 1996
ISSN: 1074-2921 WORD COUNT: 456
PUBLISHER: Charles W Henderson

Maeurer, M.J.; Gollin, S.M.; Storkus, W.J.; Swaney, W.; Karbach, J.; Martin, D.; Castelli, C.; Salter, R.; Knuth, A.; Lotze, M.T.

According to the authors' abstract of an article published in Clinical Cancer Research, "Specific CD8(+) CTL recognition of melanoma requires expression of MHC class I molecules as well as melanoma-associated peptide epitopes. Human melanoma cells may escape immune recognition by a variety of means, including global or allelic down-regulation of MHC class I molecules. Stable MHC class I cell surface expression requires delivery of cytosolic peptides into the endoplasmic reticulum by the peptide transporter molecules TAP1 and TAP2, with peptides subsequently transported to the cell surface in complexes containing MHC class I heavy chain and beta(2)-microglobulin. We have evaluated a series of mechanisms resulting in MHC class I down-regulation in a human melanoma cell line, Mz18, typed as HLA-A2(+), A3(+), B7(+), B57(+), Cw1(+), and Cw6(+) by genomic PCR analysis. The melanoma cell line Mz18 exhibits a global down-regulation of MHC class I heavy chain transcripts; beta(2)-microglobulin; the proteasome

Biosystematic Codes:
86215 Hominidae
Super Taxa:
Animals; Chordates; Vertebrates; Mammals; Primates; Humans

9/9/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11206049 BIOSIS Number: 97406049
Cloning and analysis of MAGE-1-related genes
Ding M; Beck R J; Keller C J; Fenton R G
NCI-FCRDC, P.O. Box B, Bldg. 567, Room 207, Frederick, MD 21702, USA
Biochemical and Biophysical Research Communications 202 (1). 1994. 549-555.
Full Journal Title: Biochemical and Biophysical Research Communications
ISSN: 0006-291X
Language: ENGLISH
Print Number: Biological Abstracts Vol. 098 Iss. 006 Ref. 076861
The spectrum of MAGE gene expression in the human melanoma cell line DM150 was examined using reverse transcription polymerase chain reaction and cDNA cloning. We have isolated five full-length cDNAs from DM150 which were identified as MAGE-1, MAGE-3, MAGE-12 and two previously undescribed MAGE genes, MAGE-3b and MAGE-X2. DNA sequence analysis of the coding regions of the MAGE-3b and MAGE-X2 genes revealed 83% and 88% identity with MAGE-1, while MAGE-3b was 98% homologous with the full length MAGE-3 clone. The predicted amino acid sequences of MAGE-X2 and MAGE-3b contain consensus HLA-A1 peptide binding motifs, suggesting that, like MAGE-1, they may code for tumor-associated antigens. In addition, a nonamer peptide encoded by both the MAGE-3 and MAGE-12 genes was shown by direct binding studies to contain an aggretope for HLA-A2.
Descriptors/Keywords: RESEARCH ARTICLE; HUMAN; TUMOR-ASSOCIATED ANTIGENS; HLA; DNA SEQUENCE ANALYSIS; MELANOMA CELLS; MOLECULAR SEQUENCE DATA; NUCLEOTIDE SEQUENCE; AMINO ACID SEQUENCE; POLYMERASE CHAIN REACTION; SDS-POLYACRYLAMIDE GEL ELECTROPHORESIS; ANALYTICAL METHOD
Concept Codes:
*03508 Genetics and Cytogenetics-Human
*10052 Biochemical Methods-Nucleic Acids, Purines and Pyrimidines
*10054 Biochemical Methods-Proteins, Peptides and Amino Acids
*10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines
*10064 Biochemical Studies-Proteins, Peptides and Amino Acids
*10504 Biophysics-General Biophysical Techniques
*10506 Biophysics-Molecular Properties and Macromolecules
*15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
*15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System
*18501 Integumentary System-General; Methods
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Identification of potential CTL epitopes of tumor-associated antigen MAGE-1 for five common HLA-A alleles

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Identification of CTL epitopes for tumor-specific responses is important for the development of immunotherapies to treat cancer patients. We have developed a strategy to identify potential CTL epitopes based on screening of sequences of target proteins for presence of specific motifs recognized by the most common HLA-A alleles, and identification of high affinity binding peptides using in vitro quantitative assays. A systematic analysis using the sequence of the product of the tumor-associated MAGE-1 gene has been carried out. All possible peptides of nine and ten residues, containing binding motifs for HLA-A1, -A2.1, A-3.2, -A11 and -A24 were synthesized and tested for binding using a quantitative assay. Out of 237 possible peptide/MHC combinations, 47 cases demonstrated good binding affinity (K-d ltoreq 500 nM). Several peptides were identified as good MHC binders for each one of the five HLA-A alleles studied (five for HLA-A1, 11 for HLA-A2.1, 10 for HLA-A3.2, 16 for HLA-A11 and five for HLA-A24. Furthermore, eight of these peptides were found to bind well to more than one HLA-A allele. These results have important implications for the development of immunotherapeutic vaccines to treat malignant melanoma.

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